Journal of the Formosan Medical Association (2016) 115, 609–618

Available online at www.sciencedirect.com

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ORIGINAL ARTICLE

Cost effectiveness of cancer treatment in Taiwan

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Received 21 April 2015; received in revised form 8 April 2016; accepted 13 April 2016

KEYWORDS
cancer;
cost effectiveness;
cost per quality-adjusted life year;
healthcare expenditure;
lifetime survival function;
semiparametric method

Background/Purpose: This study aims to examine the cost effectiveness of treating major cancers compared with other major illnesses in Taiwan.
Methods: We collected data on 395,330 patients with cancer, 125,277 patients with end-stage renal disease, and 50,481 patients under prolonged mechanical ventilation during 1998–2007. They were followed for 10–13 years to estimate lifetime survival functions using a semiparametric method. EuroQol five-dimension was used to measure the quality of life for 6189 cancer patients and 1401 patients with other illnesses. The mean utility values and healthcare costs reimbursed by the National Health Insurance were multiplied with the corresponding survival probabilities to estimate quality-adjusted life expectancies and lifetime costs, respectively. Data of 22,344 cancer patients under hospice care (considered as a comparison group) were used to conduct a cost-effectiveness

Conflicts of interest: The authors have no conflicts of interest relevant to this article.

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http://dx.doi.org/10.1016/j.jfma.2016.04.002

analysis. Sensitivity analysis was conducted by assuming patients without treatment survived for 2 years with a quality of life value of 0.5.
Results: The costs of care for patients under prolonged mechanical ventilation and those with end-stage renal disease were US$41,780–53,708 per quality-adjusted life year (QALY) and US$18,222–18,465 per QALY, respectively, which are equivalent to 2.17–2.79 gross domestic product (GDP) per capita per QALY and 1.18–1.25 GDP per capita per QALY. The costs of care for the nine different cancers were less than 1 GDP per capita per QALY, with those of lung, esophagus, and liver cancers being the highest. Sensitivity analysis showed the same conclusion. Lifetime risks of six out of nine cancer sites show an increased trend.
Conclusion: Cancer care in Taiwan seemed cost effective compared with that of other illnesses, but prevention is necessary to make the National Health Insurance more sustainable.

Introduction

Cancer is one of the leading causes of death worldwide and accounted for 8.2 million (22%) deaths in 2012.[1] The burden of cancer is also increasing due to the aging population in many countries, and thus cancer-related healthcare expenditures are growing rapidly. Taking Taiwan as an example, the total number of prevalent cancer cases was 463,703 in 2012, and they accounted for 10.2% of the total expenditures of the National Health Insurance (NHI) system.[2] There is thus a growing concern about the financial burden of caring for cancer patients in Taiwan, and there is a need to make cancer treatment care more efficient.[3,4]

Cost-effectiveness analysis has been recommended as a method to assess national healthcare programs in many countries.[5–7] However, the methodology has not been systematically applied to quantify how many dollars are spent per quality-adjusted life year (QALY) gained for cancer care in Taiwan's NHI system. Currently, there is an urgent need to improve resource allocation in the NHI, and to make more efficient and fair decisions regarding cancer prevention and treatment policies.

This study utilized a generalized cost-effectiveness analysis method[8] to estimate the lifetime cost per QALY for different cancer sites and for selected patients under hospice care as a comparison group to conduct a quasi-incremental cost-effectiveness ratio (quasi-ICER). The results were compared with those estimated from patients with end-stage renal disease (ESRD) and patients under prolonged mechanical ventilation (PMV). We hope that the estimates from this study can help in deriving a more sustainable policy for cancer care in Taiwan.

Methods

Study population and datasets

The study commenced after gaining approval of the Institutional Review Board of the National Cheng Kung University Hospital, Tainan, Taiwan (IRB number: ER-102-034, A-ER-101-089). Data of 395,330 patients with pathologically verified cancer registered with the Taiwan Cancer Registry and 125,277 patients with ESRD (ICD-9-CM code: 585) registered under "catastrophic illnesses" during 1998–2007 in the NHI were collected through the National Health Insurance Research Database and followed until 2007–2010, as summarized in Figure 1. The reimbursement data file obtained from the NHI of Taiwan was transformed into a research database by the National Health Research Institutes (in Chunan, Taiwan).[9] Identification numbers of all individuals in the file were encrypted to protect their privacy. These files contained detailed demographic data (including birth date and sex) and information regarding the healthcare services provided for each patient, including all payments for clinical care for outpatient visits, hospitalizations, prescription drugs, diagnoses, and intervention procedures.

In this study, nine major cancers were considered: lung (ICD-9-CM code: 162), esophagus (ICD-9-CM code: 150), liver (ICD-9-CM code: 155), stomach (ICD-9-CM code: 151), colorectal (ICD-9-CM code: 153-154), oral (ICD-9-CM code: 140-141), nasopharyngeal (ICD-9-CM code: 147), cervical (ICD-9-CM code: 180), and breast (ICD-9-CM code: 174) cancers. In addition, data of a nationwide systematic random sample of 50,481 patients who were older than 17 years and had received PMV for > 21 days (ICD-9-CM code: 518.85) during 1998–2007 were collected and they were followed up until the end of 2007.[10] In order to apply generalized cost-effectiveness analysis,[8] it is necessary to have a comparison group that is not receiving formal medical care over natural course of the disease. As all cancer treatments under internationally established guidelines can be waived from copayment under the current NHI system, it is almost impossible to recruit cancer patients who are not receiving any treatment in Taiwan. We thus assigned 22,344 cancer patients under hospice care in the comparison group to estimate survival, as they only received basic palliative care, and the quality of life (QoL) value for these individuals was assumed to be 0.4 in the analysis.[11]

Survival analysis and extrapolation to estimate life expectancy for different illnesses

All of the above patients were linked to the Taiwan Mortality Registry to obtain their survival functions via the Kaplan–Meier (K–M) estimation method.[12] These were further extrapolated to lifetime based on a semiparametric method using the age- and sex-matched referents simulated from the life tables of the Taiwan Vital Statistics.[13] Details of this method and its mathematical proofs have been described elsewhere.[10,14–17] Briefly, the method requires an assumption of constant excess hazards.[14,15,18] The estimates were obtained using integration of Survival with Quality of Life (iSQoL) statistical software (http://www.stat.sinica.edu.tw/isqol/).

Measurements of quality of life data via EuroQoL five-dimension questionnaire for estimation of quality-adjusted life expectancy

To estimate the utility value of quality of life (QoL) for these patients at different duration to dates (from the diagnosis of disease up to the date of interview), cross-sectional data of 7590 patients from 2008 to 2013 were used. Written informed consent was obtained from patients with cancer or ESRD, or those under PMV, or from their family caregivers. All the patients were receiving inpatient and/or outpatient care from 17 institutions in Taiwan. The QoL of these patients was assessed using the EuroQoL five-dimension questionnaire, which is a preference-based, generic instrument[19–21] that provides a utility value according to Taiwan's value system.[22] It ranges from 0 to 1 based on the five-dimensional health state classification, in which 0 represents the worst health status and 1 the perfect health status. In general, a cross-sectional, consecutive sample of patients was obtained, and a kernel-type smoothing method (using a moving average of the nearby 10%) was performed to estimate the mean QoL across time.[17] The QoL value after the end of the follow-up period

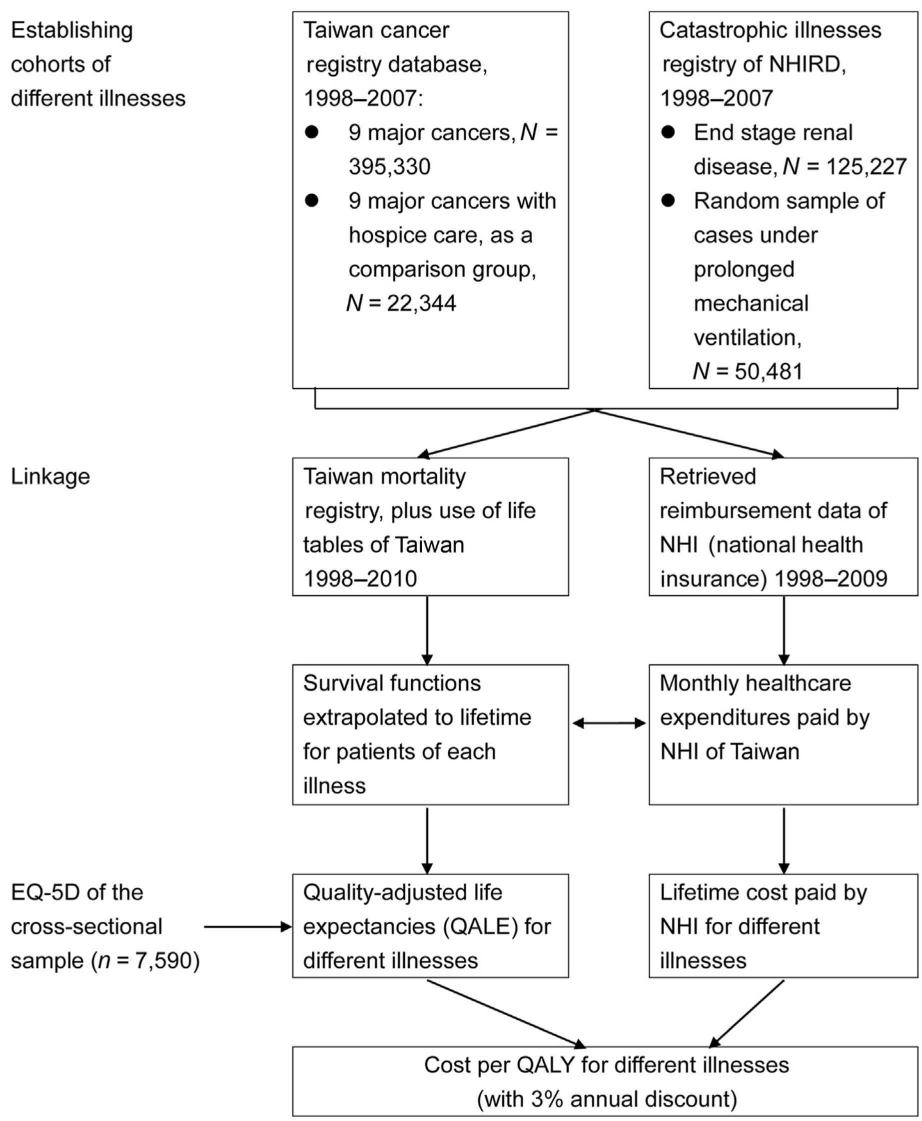

Figure 1 Flow diagram of the computation process for cost per QALY. We linked the Taiwan Cancer Registry and NHIRD to the Taiwan Mortality Registry and extrapolated the results to obtain the lifetime survival functions for patient cohorts with different illnesses, which were either adjusted with the QoL data measured in EQ-5D to obtain the QALE, or multiplied by the average monthly cost to obtain the lifetime cost after being adjusted for an annual discount rate of 3%. The cost per QALY was then calculated by dividing the lifetime cost by QALE (with 3% discount). EQ-5D = EuroQoL five-dimension; NHIRD = National Health Insurance Research Database; QALE = quality-adjusted life expectancy; QALY = quality-adjusted life year; QoL = quality of life.

Table 1 Generalized cost-effectiveness analysis for cancer care compared with that for patients under PMV and with ESRD.

	Patients with treatment					Cost-per-QALY[a]	Patients under hospice care				Quasi-ICER[b] (utility = 0.4)
	Sex	No.	Age (SD)	QALE (SE)	Lifetime cost[c] (3% discount)		No.	Age	QALE (utility = 0.4)	Lifetime cost[c] (3% discount)	
Cancer site											
Lung	Male	46,165	68.0 (11.6)	2.2 (0.0)	16,610 (891)	9491 (501)	3722	69.8 (11.7)	0.1 (0)	3139 (387)	8091 (561)
	Female	22,011	64.9 (13.2)	3.4 (0.0)	20,872 (713)	8089 (303)	2754	66.8 (12.6)	0.11 (0.01)	3619 (389)	6958 (355)
Esophagus	Male	12,111	67.7 (13.8)	2.8 (0.1)	18,313 (924)	8576 (502)	889	61.9 (13.2)	0.12 (0.01)	3028 (627)	7515 (646)
	Female	954	67.7 (13.8)	4.9 (0.2)	17,091 (1808)	4792 (553)	98	72.5 (12.9)	0.12 (0.02)	4465 (1022)	3650 (688)
Liver	Male	29,008	59.3 (13.3)	5.4 (0.1)	19,759 (1025)	4866 (262)	1880	62.9 (13.5)	0.09 (0.00)	2786 (563)	4255 (302)
	Female	10,739	62.9 (12.9)	5.7 (0.1)	19,725 (1112)	4847 (284)	875	65.3 (12.8)	0.08 (0.01)	2339 (420)	4350 (311)
Stomach	Male	23,173	67.6 (13.2)	5.5 (0.3)	17,435 (1473)	4167 (441)	1618	70.4 (12.9)	0.10 (0.00)	2219 (471)	3715 (462)
	Female	12,403	64.1 (15.2)	8.0 (0.4)	17,272 (1344)	3078 (265)	995	66.9 (15.1)	0.15 (0.01)	2608 (485)	2672 (277)
Colorectum	Male	43,731	65.4 (13.3)	9.9 (0.1)	24,677 (1741)	3428 (247)	2261	67.7 (13.2)	0.15 (0.01)	3108 (424)	3048 (258)
	Female	33,165	51.9 (12.0)	11.8 (0.1)	23,733 (1784)	2926 (226)	2097	67.1 (14.5)	0.10 (0.01)	3450 (399)	2528 (235)
Oral	Male	25,897	65.4 (13.3)	11.7 (0.2)	27,498 (1979)	3462 (262)	1469	54.7 (12.5)	0.16 (0.01)	4353 (719)	2961 (289)
	Female	2854	59.5 (15.5)	13.3 (0.2)	24,147 (1549)	2615 (179)	196	67.2 (15.3)	0.11 (0.01)	3754 (777)	2233 (198)
Nasopharynx	Male	10,459	49.8 (13.2)	11.9 (0.3)	29,809 (3105)	3578 (378)	453	54.6 (13.6)	0.26 (0.02)	5783 (840)	2955 (402)
	Female	3701	49.2 (13.8)	18.0 (0.4)	30,225 (3066)	2676 (274)	179	56.6 (13.8)	0.52 (0.03)	5398 (782)	2273 (291)
Breast	Female	59,412	51.2 (12.1)	21.3 (0.2)	28,180 (1452)	2054 (106)	1718	57.3 (13.5)	0.34 (0.01)	5007 (508)	1720 (111)
Cervix	Female	59,547	51.3 (14.6)	25.9 (0.3)	17,645 (1147)	1107 (72)	1140	62.5 (14.5)	0.28 (0.02)	4809 (606)	816 (88)
PMV	Male	30,298	71.1 (14.6)	0.8 (0.1)	25,225 (2517)	41,780	—	—	—	—	41,780
	Female	20,183	73.2 (14.5)	0.8 (0.1)	32,260 (3292)	53,708	—	—	—	—	53,708
ESRD	Male	61,241	60.4 (15.0)	7.5 (0.1)	129,658 (2885)	22,714 (534)	—	—	0.20	—	18,222
	Female	64,036	62.0 (14.6)	7.7 (0.1)	138,487 (3248)	24,180 (605)	—	—	0.20	—	18,465

ESRD = end-stage renal disease; ICER = incremental cost-effectiveness ratio; PMV = prolonged mechanical ventilation; QALE = quality-adjusted life expectancy; QALY = quality-adjusted life year; SD = standard deviation; SE = standard error of mean.

[a] Cost per QALY; both QALE and lifetime cost were applied (with 3% discount).

[b] Quasi-ICER, calculated based on the difference in comparison to patients under hospice care, and both QALE and lifetime cost were applied (with 3% discount).

[c] Lifetime cost (in US dollars at a 3% discount rate) paid by the National Health Insurance of Taiwan.

was assumed to be the same as the average of the last 10% of measurements through smoothing. The lifetime survival probabilities of a cancer under study were multiplied (or adjusted) with the QoL utility values to obtain a quality-adjusted survival curve. The total area under this curve was the quality-adjusted life expectancy (QALE),[17] as shown in Figure A1.

Lifetime healthcare expenditures paid by the NHI for different illnesses

The lifetime healthcare expenditures were estimated by counting the monthly average dollars reimbursed by the NHI during 1998–2009 for these patients, from the day of validated diagnosis or hospice care to the end of life or till being censored.[23] The calculation process was as follows. The average monthly expenditures, including the costs of inpatient, outpatient, and emergency care, were summed for each patient. Each month, the aggregate expenditure was divided by the number of patients who were still alive to estimate the monthly average costs to the NHI. Annual NHI expenditures were first adjusted to the 2010 monetary value using the Consumer Price Index. The adjusted annual expenditure was discounted at a rate of 3% following the recommendation of the US Cost-Effectiveness Panel.[5] The total average monthly expenditures were multiplied by the monthly survival probabilities for each illness over a lifetime. All the estimated monetary values were summed to obtain the lifetime healthcare expenditure for each major catastrophic illness, as shown in Figure A2.

Estimation of cost per QALY for different illness groups

The ICER was estimated using the following formula: (average total lifetime cost of all treatment minus that of hospice care)/estimated QALE with all treatments minus that of hospice care. We adopted the criterion suggested by WHO-CHOICE (World Health Organization-CHOosing Interventions that are Cost Effective), and applied one to three times the gross domestic product (GDP) per capita as the threshold for cost effectiveness.[24] Taiwan's GDP per capita in 2010 was US$19,278.[25]

Similarly, patients with ESRD were also waived from copayment under the NHI and usually passed away within 3 months after discontinuing dialysis. We thus assumed 3 months of life expectancy for ESRD patients, and the utility value was assumed to be 0.4 under palliative or hospice care. Again, because PMV patients require a ventilator every day for at least 6 hours to remain alive, and they continued using a ventilator for >21 days and were waived from copayment, we assumed immediate mortality for PMV patients without mechanical ventilation.[10]

Uncertainties and validation of the extrapolation method for different illnesses

In estimating uncertainty and validation, an *ex post* approach was used instead of the conventional *ex ante*. Survival data were based on real follow-up for at least 10–13 years. The healthcare expenditures were directly retrieved from the reimbursement data files of the NHI system. The standard errors of the mean were calculated by the bootstrap method for 100 repeated samples in these parameters, including QALE and lifetime cost. Since survival is the most important determinant of lifetime cost, we validated our extrapolation method in the following manner: Survival of subcohorts of patients with different illnesses between 1998 and 2003 was analyzed by the K–M method, and then these results were extrapolated to the end of 2010 by our semiparametric method, which were compared with the K–M estimates of the actual 13 years of follow-ups (namely, from 1998 to 2010). Assuming that the K–M estimates were the gold standard, we calculated the relative biases for subcohorts with different illnesses and cancer. The relative bias is defined as follows:

relative bias = (estimate from extrapolation − K–M estimate)/K–M estimate. (1)

Sensitivity analysis for cost-effectiveness

As the life span of patients under hospice care might be too short, we assumed an average life expectancy of 2 years and an average QoL value of 0.5 after the diagnosis of each type of cancer in the "no treatment scenario" to conduct a sensitivity analysis for cost effectiveness of cancer care. To be fair about the healthcare expenditures of cancer care for such a

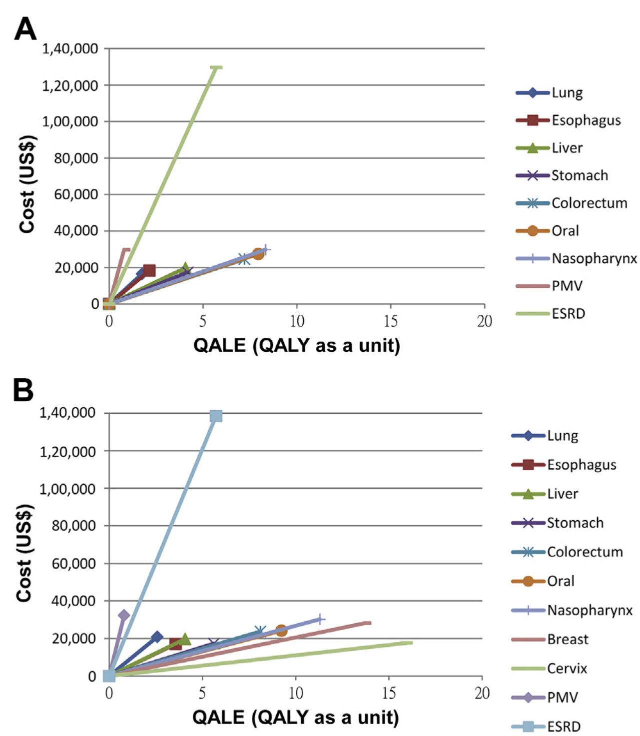

Figure 2 Comparison of cost per QALY (3% discount) for different types of cancers, patients under PMV, and patients with ESRD, stratified by gender: (A) males and (B) females. ESRD = end-stage renal disease; PMV = prolonged mechanical ventilation; QALE = quality-adjusted life expectancy; QALY = quality-adjusted life year.

scenario, we also assumed that the lifetime costs of cancer patients would be the same as those of the hospice care.

Estimation of cumulative incidence rates of major cancers

We used the Catastrophic Illnesses Registry for the period 1998–2010 to calculate the incidence rates of major cancers. The cumulative incidence rate (CIR) from age 20 years to 79 years was calculated to estimate the lifetime risk of a specific illness, as follows:

$$CIR = 1 - \exp[-\Sigma_i(IR_i)\cdot(\Delta t_i)] \quad (2)$$

where IR_i represents the age-specific incidence rate and Δt_i indicates the range of each age stratum.

Results

We excluded about 1% of invited patients who were totally unable to communicate with research assistants for the QoL interview, plus 9% who refused to be interviewed. Of the nine different cancers studied, even though patients with cervical cancer were not the youngest at diagnosis, their QALE was the longest, i.e., 25.9 QALY (Table 1 and Figure 2). Patients under hospice care were usually older and were responsible for less healthcare expenditures than those under regular treatment. Nasopharyngeal cancer represented the highest lifetime healthcare expenditure in males and females, with estimates of US$29,809 and US$30,225, respectively. All of the nine different cancers were reimbursed for $<$ 1 GDP per capita per QALY. Lung, esophagus, and liver cancers showed the highest cost per QALY, with 0.42–0.49 GDP, 0.25–0.44 GDP, and 0.24–0.25 GDP per capita per QALY, respectively. The estimated quasi-ICER for these cancers ranged from 0.36 to 0.42 GDP, from 0.19 to 0.39 GDP, and from 0.22 to 0.23 GDP per capita per QALY, respectively. There is a general trend of shorter QALE being associated with higher cost per QALY. ESRD caused the highest life-time healthcare expenditure at US$129,658–138,487. PMV had the highest cost per QALY followed by ESRD, which were estimated at 2.17–2.79 GDP and 1.18–1.25 GDP per capita per QALY, respectively (Table 1 and Figure 2).

The results obtained to validate our semiparametric method show that the relative biases of extrapolation from the end of the 6^{th} year to that of the 13^{th} year were all below 11% (Table A1), which would be even smaller after our actual follow-up for 13 years. In addition, the sensitivity analysis of cost effectiveness for cancer care showed a consistent result of less than 1 GDP per capita, or 0.04–0.86 GDP per capita, for care of cancers of different organ systems in comparison with no treatment. We found that the top three quasi-ICERs were US$16,631 and US$10,520 for male and female lung cancer, US$12,738 and US$4,801 for male and female esophageal cancer, and US$5440 and US$5555 for male and female liver cancer, respectively (Table A2). The lifetime risk (CIR_{20-79}) of major cancers has continually increased over the past decade, except that for stomach, nasopharyngeal, and cervical cancers (Table 2).

Table 2 CIR_{20-79} (%) of major cancers stratified by gender and calendar years.

Site of cancer	Gender	1998–2002	2003–2007	2008–2010
Lung	Male	5.18	5.72	6.05
	Female	2.54	2.77	3.15
Esophagus	Male	1.06	1.34	1.55
	Female	0.11	0.11	0.12
Liver	Male	5.99	6.67	6.80
	Female	2.66	2.95	3.12
Stomach	Male	2.60	2.37	2.08
	Female	1.42	1.22	1.13
Colorectum	Male	4.68	5.53	6.30
	Female	3.82	4.07	4.36
Oral	Male	2.05	2.63	2.99
	Female	0.30	0.33	0.38
Nasopharynx	Male	1.02	0.92	0.88
	Female	0.42	0.32	0.29
Breast	Female	4.68	5.44	6.52
Cervix	Female	3.32	1.94	1.37

CIR_{20-79} = cumulative incidence rate from age 20 years to 79 years.

Discussion

We found that the cost per QALY for treating cancer at different major organ sites is $<$ 1 GDP per capita in Taiwan, from the perspective of the NHI. The following arguments support this inference: First, to ensure the quality of diagnoses, we included only cancer patients verified with pathology (except liver cancer[26]) and registered with the Taiwan Cancer Registry; patients who were hospitalized with PMV and those with ESRD were all registered in the Catastrophic Illnesses Registry, and thus their diagnoses had been validated by at least two specialists to ensure no abuse with regard to waiving copayments. Second, we ensured that all the extrapolations were made through the verification of the existence of a "constant excess hazard," which can be obtained by showing a straight line after taking the logit transform of the survival ratio between the index and age- and gender-matched referents.[14–16,18] Moreover, we further validated these estimations by extrapolating the survival for the first 6 years up to 13 years, and showed that there was generally $<$ 11% error in comparison with the actual survival based on the K–M method (Table A1). As the survival functions of all patients in this study (except those under PMV) were estimated based on $>$ 13 years of follow-up, at which the majority of cancer patients would be deceased, the estimation of life expectancy would be more accurate. Third, because all patients registered in the Catastrophic Illnesses Registry of the NHI are waived from any copayments, all related costs for treating these illnesses would be very comprehensive and comparable. Fourth, we assigned 22,344 cancer patients under hospice care to a comparison group for quasi-ICER analysis, and the results appeared similar (Table 1). We also used cancer patients without treatment as another comparison group to conduct a sensitivity analysis of cost effectiveness of care for cancers of different organ systems, which showed 0.04–0.86 GDP per capita (Table A2).

Namely, all the quasi-ICERs were less than 1 GDP per capita. Therefore, we tentatively concluded that the cost per QALY of all cancer management is less than that for PMV and ESRD. As all these values of cancer management were $<$ 1 GDP of Taiwan per capita per QALY, they are relatively cost effective based on the criteria proposed by WHO.[24]

Based on qualitative analysis, we attribute the apparently low cancer care cost to the following reasons: most of the related hospitals are nonprofit organizations in Taiwan; the NHI has adopted and encouraged hospice care for terminal cancer patients since 1996; the country currently spends only $\sim$6.9% of GDP on total healthcare expenditure, which is lower than the figures for most countries of the Organization for Economic Cooperation and Development.[27] Nonetheless, continued efforts to develop more cost-effective clinical guidelines for cancer care[3,4] should be encouraged, in order to ensure the sustainability of the NHI system.

Financial burdens of cancer care also depend on the incidence rates. For direct comparison, we quantified the lifetime risk of major cancers by calculating the CIR_{20-79}, which shows a consistent rising trend over the past decade (Table 2), except for cervical, nasopharyngeal, and stomach cancers. Therefore, total healthcare expenditures would still increase in the future, even if we were able to hold down cost per QALY by sticking to more cost-effective management guidelines. This issue requires special attention, especially with regard to prevention, if we hope to achieve a system of sustainable and affordable cancer care.[3,28] In addition to reducing occupational and environmental risks, stakeholders and care providers may consider tackling the issue from the whole cycle of care.[29] Cancer screening for early detection and prompt treatment may be one of the viable choices, as has been demonstrated in case of cervical cancer.[30,31]

Limitations

Our study has the following limitations. First, because the reimbursement data we used were only up to 2009, we were unable to include many new medications and treatments that might be more expensive than those used during this period. For example, some molecular target therapies have been covered by the NHI in Taiwan since 2011, such as bevacizumab and cetuximab for colorectal cancer, and sorafenib for liver cancer. The application criteria for some of these therapies were broadened after 2011, such as those for erlotinib and gefitinib for lung cancer, and trastuzumab for breast cancer.[32] Therefore, the lifetime health expenditure or cost per QALY for colorectal, liver, and several other cancers treated with these new medications could be higher after 2009. Careful monitoring of such expenditures is thus necessary in the future to ensure the efficiency and equity of the NHI system. Second, during extrapolation, we assumed that the QoL of the patients remained the same as that measured at the end of the follow-up period. However, this assumption could result in an overestimation of the QALE, because the actual QoL might gradually decline with age and increasing comorbidity.[33,34] In general, such an overestimation would be higher in elderly patients than that in younger ones, which must be considered if we are comparing different diseases with various ages at diagnosis. However, because we followed these patients for 13 years and applied the same estimation method for all diseases in this study, the bias might not be too large. Third, as most of the interviewed patients were recruited from clinics, their general conditions were probably better than those confined at home or in institutions. Our results might thus have overestimated the QoL and QALE. However, since we applied the same strategy for recruitment of patients with cancers of different organ systems, such an overestimation might not have produced too much bias among them. Finally, this study is conducted from the viewpoint of a single payer, namely, the NHI. As the financial difficulty has become heavier, bundle payment (e.g., Diagnosis Related Group) has been adopted step by step to slow down the growth of financial demand, which might result in a potential bias on the estimation of reimbursement costs. However, since cancer treatment is not yet included in the Diagnosis-Related Group payment system in Taiwan, and bundle payment would usually decrease or underestimate the costs, such a system will not change the conclusion of this study. Instead, future studies must take such a potential impact into consideration.

Conclusion

In conclusion, treatments of major cancers in Taiwan appeared affordable up to 2009 if we compared them with those of patients under PMV or with ESRD, or applied a cutoff point of 1 GDP per capita per QALY. However, since the incidence rates of major cancers have continually increased over the past decade, except those for stomach, nasopharyngeal, and cervical cancers, proactive prevention remains the key approach to make the NHI more sustainable. We recommend that future studies consider evaluating the cost effectiveness of different prevention programs for direct comparison across prevention,[28] diagnosis and treatment, rehabilitation, and alternative medicine.[35]

Acknowledgments

The authors thank the Department of Statistics, Ministry of Health and Welfare of Taiwan, for its assistance in the acquisition and linkage of all related national databases. They also thank the Cancer Data Bank of National Cheng Kung University Hospital for retrieving the cancer case database. The authors thank J.M. Sung, Department of Internal Medicine, National Cheng Kung University Hospital, and L. Chen, Institute of Population Health Sciences, National Health Research Institutes, for their kind assistance in collecting and sharing of QoL data of their patients; and Dr Donatus U. Ekwueme, Division of Cancer Prevention and Control, US Centers for Disease Control and Prevention, for providing constructive comments and helping in editing this manuscript. This work was partially supported by grants from the National Science Council of Taiwan (NSC 99-2628-B-006-036-MY3, NSC 101-3114-Y-006-001, NSC 102-2314-B-006-029-MY2, and NSC 102-2811-B-006-018), Ministry of Health and Welfare of Taiwan (DOH 102-TD-C-111-003 and MOHW103-TD-B-111-069), and the Top University Project to the National Cheng Kung University from the Ministry of Education of Taiwan. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Appendix

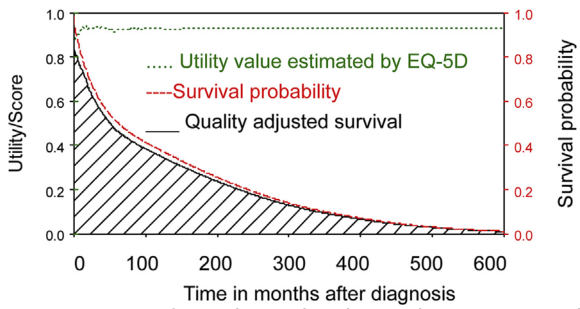

Figure A1 QALE for males with colorectal cancer. A total of 43,731 patients were followed for 13 years, and their data were extrapolated throughout lifetime to obtain the survival function, which was adjusted by the utility values measured with the EQ-5D ($N = 817$). The total area under the quality-adjusted survival curve (shaded areas) was then summed up as the QALE, which was 9.9 ± 0.1 QALYs. EQ-5D = EuroQoL five-dimension; QALE = quality-adjusted life expectancy; QALY = quality-adjusted life year.

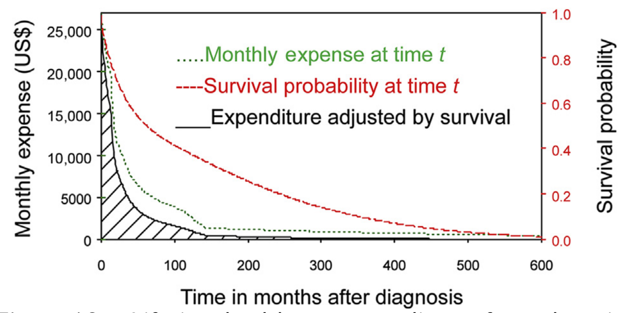

Figure A2 Lifetime healthcare expenditures for males with colorectal cancer. The monthly survival probability ($N = 43,731$) was multiplied by the monthly expenses and summed up for a lifetime (shaded areas), which amounts to US$24,677 ± 1741 (3% discount).

Table A1 Estimates of mean survival years in 13 years of follow-up using the semiparametric method of extrapolation based on the first 6 years of follow-up data with a high censored rate, compared with the K–M estimates of 13 years of follow-up for patients with major cancers and ESRD.

Illness	Gender	Cohort size	Age at diagnosis (SD)	Censored rate (%)	13 y survival based on K–M estimate (SE) (mo)	Extrapolation based on the first 6 y of follow–up (SE) (mo)	Relative bias (%)[a]
Cancer site							
Lung	Male	25,118	67.8 (11.3)	24.3	22.9 (0.3)	23.3 (0.5)	1.8
	Female	11,355	64.5 (13.0)	31.0	29.0 (0.5)	29.2 (0.9)	0.9
Esophagus	Male	6099	60.6 (12.6)	28.5	25.9 (0.5)	28.8 (1.0)	10.8
	Female	534	68.1 (13.3)	37.5	42.3 (2.6)	41.3 (4.4)	−2.4
Liver	Male	15,719	58.7 (13.4)	43.9	44.1 (0.5)	44.8 (1.8)	1.8
	Female	5730	62.2 (13.1)	46.1	46.2 (0.7)	43.1 (2.5)	−6.6
Stomach	Male	13,719	67.2 (13.1)	44.7	52.0 (0.6)	51.2 (1.3)	−1.5
	Female	7042	63.5 (15.2)	49.6	61.5 (0.8)	60.8 (1.9)	−1.1
Colorectum	Male	22,744	65.0 (13.2)	64.7	77.6 (0.4)	76.6 (2.1)	−1.3
	Female	17,095	64.1 (14.2)	67.1	84.4 (0.4)	80.3 (2.8)	−4.9
Oral	Male	12,998	51.7 (12.2)	64.3	78.7 (0.5)	75.6 (1.7)	−3.9
	Female	1467	59.0 (15.8)	71.2	91.3 (1.6)	92.6 (4.6)	1.4
Nasopharynx	Male	6065	49.5 (13.2)	71.9	88.9 (0.8)	88.9 (2.2)	0.0
	Female	2161	48.8 (13.8)	77.9	103.4 (1.4)	96.2 (3.9)	−7.0
Breast	Female	29,925	50.5 (12.2)	88.5	123.6 (0.3)	120.0 (2.2)	−2.9
Cervix	Female	36,749	51.6 (14.3)	90.9	133.4 (0.3)	133.9 (0.8)	0.4
ESRD	Male	31,459	58.6 (15.1)	63.3	76.6 (0.3)	75.9 (0.7)	−0.9

ESRD = end-stage renal disease; K–M = Kaplan–Meier; SD = standard deviation; SE = standard error of mean.
[a] Relative bias = (estimate from extrapolation − K–M estimate)/K–M estimate.

Table A2 Sensitivity analysis of cost effectiveness for care of cancers of different organ systems, stratified by sex.

Cancer site	Sex	Patients without treatment		Quasi-ICER[a]
		QALE (survival = 2 y; utility = 0.5)	Lifetime cost[b] (3% discount)	
Lung	Male	1.0	3139	16,631
	Female	1.0	3619	10,520
Esophagus	Male	1.0	3028	12,738
	Female	1.0	4465	4801
Liver	Male	1.0	2786	5440
	Female	1.0	2339	5555
Stomach	Male	1.0	2219	4696
	Female	1.0	2608	3139
Colorectum	Male	1.0	3108	3446
	Female	1.0	3450	2828
Oral	Male	1.0	4353	3305
	Female	1.0	3754	2458
Nasopharynx	Male	1.0	5783	3251
	Female	1.0	5398	2398
Breast	Female	1.0	5007	1813
Cervix	Female	1.0	4809	855

ICER = incremental cost-effectiveness ratio; QALE = quality-adjusted life expectancy, the unit is year.

[a] Quasi-ICER, calculated based on the difference between patients with and without treatment, and both QALE and lifetime cost were applied (with 3% discount).

[b] Estimation of lifetime cost (in US dollars) assumed that the monthly cost of "no treatment scenario" is the same as that of hospice care.

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